

mucous membrane without being solubilized, said active agent being contained in said liquid droplets, or in said sheath, or in both said liquid droplets and said sheath.

54. The method of claim 53, wherein the solubility of the more soluble component(s) is at least  $10^{-3}$  M to  $10^{-6}$  M and the solubility of the less soluble component(s) is at least  $10^{-6}$  M to  $10^{-10}$  M.

55. The method of claim 53, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between 10 M and  $10^7$  M.

56. The method of claim 55, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between  $10^2$  M and  $10^6$  M.

57. The method of claim 55, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between  $10^3$  M and  $10^5$  M.

58. The method of claim 53, wherein the preparation permeating through said skin or mucous membrane has a permeability of at least 0.001% of the permeability of small molecules, which permeate essentially without being impeded.

59. The method of claim 53, wherein the permeation capability relative to reference particles  $P_{(\text{transfer.})}/P_{(\text{refer.})}$ , the reference particles being water, is between  $10^{-5}$  M and 1 M.

60. The method of claim 59, wherein the permeation capability relative to reference particles  $P_{(\text{transfer.})}/P_{(\text{refer.})}$ , the reference particles being water, is between  $10^{-4}$  M and 1 M.

61. The method of claim 59, wherein the permeation capability relative to reference particles  $P_{(\text{transfer.})}/P_{(\text{refer.})}$ , the reference particles being water, is between  $10^{-2}$  M and 1 M.
62. The method of claim 53, wherein the content of said at least one active agent in the preparation does not change significantly during transport through the skin or mucous membrane.
63. The method of claim 62, wherein the sheath is a double layer.
64. The method of claim 53, wherein the vesicle radius of the transfersome is between about 25 nm and about 500 nm.
65. The method of claim 64, wherein the vesicle radius of the transfersome is between about 50 nm and about 200 nm.
66. The method of claim 64, wherein the vesicle radius is between about 80 nm and about 100 nm.
67. The method of claim 53, wherein said amphiphilic components comprise lipids of different polarity.
68. The method of claim 67, wherein the less polar amphiphilic lipid component is a phospholipid, and a second, more soluble amphiphilic component is an active ingredient, the concentration of the more soluble component(s) being between 0.01% by weight and 15% by weight.
69. The method of claim 68, wherein the concentration of the more soluble component(s) is between 0.1% by weight and 10% by weight.
70. The method of claim 68, wherein the concentration of the more soluble component(s) is

between 0.1% by weight and 10% by weight.

70. The method of claim 68, wherein the concentration of the more soluble component(s) is between about 0.5% by weight and 3% by weight.

71. The method of claim 68, wherein the total lipid concentration being between about 0.5% by weight and 15% by weight.

72. The method of claim 68, wherein the total lipid concentration being between about 1% by weight and 10% by weight.

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cont.

73. The method of claim 53, wherein at least one amphiphilic lipid component is selected from the group consisting of a diacyl or a dialkyl glycerophosphoethanolamino azo polyoxyethylene derivative, a didecanoyl phosphatidyl choline, a diacyl phosphooligomaltobionamide, a glyceride, a glycerophospholipid, a isoprenoid lipid, a sphingolipid, a steroid, a sterol, a half protonated liquid fatty acid, a phosphatidyl choline, a phosphatidyl ethanolamine, a phosphatidyl glycerol, a phosphatidyl inositol, a phosphatid acid, a phosphatidyl serine, a sphingomyelin, a sphingophospholipid, a glycosphingolipid, a cerebroside, a ceramide polyhexoside, a sulfatide, a sphingoplasmalogen, a ganglioside, and a glycolipid.

74. The method of claim 53, wherein at least one amphiphilic lipid component is a synthetic lipid.

75. The method of claim 53, wherein at least one amphiphilic lipid component is selected from the group consisting of a sulfur containing lipid and a hydrocarbon-containing lipid which forms stable structures.

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76. The method of claim 53, wherein ~~at least~~ one amphiphilic lipid component is an identical

77. The method of claim 75, wherein the stable structures are double layers.
78. The method of claim 53, wherein at least one amphiphilic lipid component is selected from the group consisting of a dioleoyl phospholipid, a dilinoyl phospholipid, a dilinolenyl phospholipid, a dilinoleoyl phospholipid, a dilinolinoyl phospholipid, a diarachinoyl phospholipid, a dilauroyl phospholipid, a dimyristoyl phospholipid, a dilalmitoyl phospholipid, a distearoyl phospholipid, and corresponding dialkyl or sphingosin derivatives thereof.
79. The method of claim 73, wherein at least glycosphingolipid is selected from the group consisting of cerebroside, ceramide polyhexoside, sulfatide and sphingoplasmaologen.
80. The method of claim 53, wherein the less soluble amphiphilic lipid component is selected from the group consisting of a myristoleoyl, a palmitoleoyl, a petroselinyl, a petroselaidyl, a oleoyl, elaidyl, a cis- or trans- vaccenoyl, a linoyl, a linolenyl, a linolaidyl, a octadecatetraenoyl, a gondoyl, a eicosaenoyl, a eicosadienoyl, a eicosatrienoyl, a arachidoyl, a cis- or trans-docosaenoyl, a docosadienoyl, a docosatrienoyl, a docosatetraenoyl, a caproyl, a lauroyl, a tridecanoyl, a myristoyl, a pentadecanoyl, a palmitoyl, a heptadecanoyl, a stearoyl or a nonadecanoyl, a glycerophospholipid, a glycolipid, an acyl lipid, and an alkyl lipid.
81. The method of claim 53, wherein the total content of the amphiphilic components is between 0.01 and 40% by weight of the preparation.
82. The method of claim 75, wherein the total content of the amphiphilic components is between about 0.1 and 15% by weight.
83. The method of claim 75, wherein the total content of the amphiphilic components is between about 1 and 10% by weight.

84. The method of claim 53, wherein the active ingredient is selected from the group consisting of an adrenocorticotrophic agent, a  $\beta$ -adrenolytic agent, an androgen, an antiandrogen, an anti-parasitic, an anabolic, an anesthetic, an non-narcotic analgesic, an analeptic, an anti-allergic, an anti-arrhythmic, an anti-arteriosclerosis, an anti-asthmatic, a bronchospasmolytic agent, an antibiotic, an anti-depressive agent, an anti-psychotic agent, an anti-diabetic agent, an antidote, an anti-emetic, an anti-epileptic, an anti-fibrinolytic, an anti-convulsive agent, an anti-cholinergic agent, an enzyme, a coenzyme, a coenzyme inhibitor, an antihistamine, an antihypertensive drug, a biological activity inhibitor, an antihypotensive agent, an anticoagulant, an anti-mycotic, an antimyasthenic agent, an active ingredient against Parkinson's disease, an active ingredient against Alzheimer's disease, an anti-phlogistic, a anti-pyretic, an anti-rheumatic agent, an antiseptic, a respiratory analeptic, a respiratory stimulating agent, a broncholytic, a cardiotonic agent, a chemotherapeutic agent, a coronary dilator, a cytostatic agent, a diuretic, a ganglion blocker, a glucocorticoid, a therapeutic agent for influenza, a hemostatic agent, a hypnotic agent, an immunoglobulin, a bioactive carbohydrate, a contraceptive, a migraine agent, a mineral corticoid, a morphine antagonist, a muscle relaxant, a narcotic, a neural therapeutic agent, a CNS therapeutic agent, a nucleotide, a polynucleotide, a neuroleptic agent, a neuron transmitter, a neuron transmitter antagonist, a peptide, a peptide derivative, an ophthalmic agent, a para-sympathomimetic or para-sympathicolytic agent, a protein, a protein derivative, a psoriasis/neurodermatitis agent, a mydriatic agent, a mood elevator, a rhinological agent, a sleeping draft, a sleeping draft antagonist, a sedative, a spasmolytic, a tuberculosis agent, a urological agent, a vasoconstrictor, a vasodilator, a virostatic agent, a wound-healing agent, and a non-steroidal antiinflammatory agent.

85. The method of claim 53, wherein the active ingredient is a nonsteroidal anti-inflammatory drug selected from the group consisting of diclofenac, ibuprofen, and a lithium, sodium, potassium, cesium, rubidium, ammonium, monoethyl, dimethyl, trimethylammonium or ethylammonium salt thereof.

86. The method of claim 53, wherein the preparation comprises consistency modifiers

selected from the group consisting of a hydrogel, an antioxidant selected from the group consisting of a probucol, a tocopherol, a BHT, an ascorbic acid, a desferroxamine or a stabilizer selected from the group consisting of a phenol, a cresol, and a benzyl alcohol.

87. The method of claim 53, wherein the active ingredient is a growth regulating substance.

88. The method of claim 53, wherein the active ingredient is selected from the group consisting of an insecticide, a pesticide, a herbicide or a fungicide.

89. The method of claim 53, wherein the active ingredient is an allurement.

90. The method of claim 53, further comprising one or more solubilizing components in an amount effective to provide adequate deformability to said transfersomes, such that said transfersomes are capable of passing through said skin or mucous membrane without being solubilized, the amount of solubilizing components included in said preparation being less than 0.1 mole percent at which the solubilizing point of the enveloped droplets is reached, based on the content of said amphiphilic lipid components.

### REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated April 20, 2001 with respect to the above-identified application are respectfully requested in view of the amendments and remarks set forth below.

### Status of Claims

Claims 1, 3-13, 15-21 and 34-48 have been cancelled without prejudice to further prosecution in another application. Upon entry of this amendment claims 22-33, 49-52 and 53 - 90 are pending. Claims 53-90 are directed to methods of treatment by administering to the skin or